UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

IN RE: VALSARTAN, LOSARTAN, AND IRBESARTAN PRODUCTS LIABILITY LITIGATION	**MDL No. 2875** **HON. ROBERT B. KUGLER** **CIVIL NO. 19-2875 (RBK)**
THIS DOCUMENT RELATES TO ALL CASES	

STATEMENT OF UNDISPUTED MATERIAL FACTS

TORRENT

I. Torrent's Structure and Role in the Manufacture of Valsartan

1. Torrent Pharmaceuticals Limited is an Indian company that supplies pharmaceutical products to countries throughout the world, including the United States. (Torrent Ex. 4, Gegenheimer Dep. 20:19–21:10; Torrent Ex. 3, Chitty Dep. 190:2–3.)

2. Torrent Pharma, Inc. is the United States subsidiary of Torrent Pharmaceuticals Limited which, along with Torrent Pharmaceuticals Limited has responsibility for products in the United States market (Torrent Ex. 4, Gegenheimer Dep. 20:19–21:10; Torrent Ex. 3, Chitty Dep. 190:15–191:7.) Sanjay Gupta is the President and Chief Executive Officer of Torrent Pharma, Inc. (Torrent Ex. 5, Gegenheimer Dep. 644:10–11.)

3. Sushil Jaiswal, who testified as a 30(b)(6) corporate representative, is the Executive Director of Global Quality and Regulatory Affairs for Torrent Pharmaceuticals Limited. (Torrent Ex. 1, Jaiswal Dep., 22:18–23:9.)

4. Kelly Gegenheimer, who testified as a 30(b)(6) corporate representative, is the Vice President of Sales of Torrent Pharma, Inc. (Torrent Ex. 4, Gegenheimer Dep. 38:20–20–24.)

5. Torrent manufactured finished dose valsartan tablets, amlodipine and valsartan tablets, amlodipine, valsartan, and hydrochlorothiazide tablets, and valsartan and hydrochlorothiazide tablets for the United States market between 2015 and 2018. (Torrent Ex. 9, TORRENT-MDL-2875-00133890; Torrent Ex. 1, Jaiswal Dep. 78:15–18; Torrent Ex. 2, Jaiswal Dep. 373:4–8.) Torrent's corporate representative agreed that, as the finished dose manufacturer, Torrent bore ultimate responsibility for the manufacture of a "quality" drug. (Torrent Ex. 2, Jaiswal Dep. 736:9–737:4.)

a. Specifically, Mr. Jaiswal agreed that Torrent was responsible for ensuring that Torrent's facilities were manufacturing "quality" drugs. (*Id.* at 697:11–24.)

b. In addition, Mr. Jaiswal agreed that Torrent is responsible for testing the product before putting it on the market. (*Id.* at 736:17–21.)

6. The DMF holder for the valsartan active pharmaceutical product (API) used by Torrent in its finished dose valsartan was Zhejiang Huahai Pharmaceuticals (ZHP). (Torrent Ex. 1, Jaiswal Dep. 67:14.) ZHP used two routes of synthesis to manufacture valsartan API, which Torrent referred to as the "old process" and "new process." (*Id.* at 67:6–19.)

7. To manufacture finished dose valsartan for the United States market, Torrent purchased only valsartan API batches designated with the letter "C" (hereinafter "C code") from ZHP to indicate that they were synthesized with the "old" process. (Torrent Ex. 9, TORRENT-MDL-2875-00133890 at 5; Torrent Ex. 1, Jaiswal Dep. 68:4–7.) The "old"

process was the manufacturing process that used triethylamine (TEA). (Torrent Ex. 9, TORRENT-MDL-2875-00133890.)

8. Valsartan API batches designated with the letter "D" (hereinafter "D code") were synthesized with the "new" process. (*Id.*) The "new" process was the manufacturing process that used zinc chloride. (*Id.*)

II. The Discovery and Response to Nitrosamine Impurities by Torrent

9. On June 20, 2018, ZHP notified Torrent of a genotoxic impurity in its valsartan API. (Torrent Ex. 8, ZHP00496536.)

10. Torrent placed its valsartan on hold but did not perform any testing for genotoxic impurities at this time. (*Id.* at 31; Jaiswal Dep. 226:17–227:2.)

11. On June 26, 2018, ZHP notified Torrent that its D code valsartan API manufactured with the "new" (zinc chloride) process contained NDMA. (Torrent Ex. 8, ZHP00496536; Torrent Ex. 1, Jaiswal Dep. 227:3–228:1.) Accordingly, Torrent concluded that its C code valsartan products manufactured with the "old" TEA process API, including those manufactured for the United States market, were not contaminated with NDMA. (Torrent Ex. 8, ZHP00496536; Torrent Ex. 1, Jaiswal Dep. 227:3–228:1.)

12. At this time, Torrent did not perform any testing to confirm that ZHP was correct; rather, Torrent relied on the representation from ZHP and chose not to recall its valsartan. (Torrent Ex. 1, Jaiswal Dep. 230:4–17, 23:41–1–10.) Customers in the United States could therefore purchase Torrent valsartan made from ZHP C code API. (*Id.*) However, ZHP was incorrect about the absence of NDMA in its C code (old process) valsartan API. (Torrent Ex. 1, Jaiswal Dep. 234:24–235:3.)

13. On July 7, 2018, Torrent carried out an impact assessment for the United States market and concluded that it manufactured 129 batches of finished dose valsartan using API from C code batches indicating that they used the "old process" with triethylamine. (Torrent Ex. 10, TORRENT-MDL2875-0072713.) Torrent determined that it did not manufacture any finished dose valsartan using API from D code batches indicating that they used the "new process" with zinc chloride. (*Id.*)

14. On July 21, 2018, Torrent confirmed that there were 103 batches in the market which were manufactured with the C code of API, indicating that they used the "old process" with triethylamine. (*Id.*)

15. By August 3, 2018, ZHP notified Torrent that API manufactured with the "old process," that is, C code API, contained NDMA. (Torrent Ex. 1, Jaiswal Dep. 121:23–123:22, 138:5–8.)

16. On August 17, 2018, the FDA informed Torrent that five batches of its valsartan finished dose product were made from C code API containing NDMA above acceptable levels. (Torrent Ex. 10, TORRENT-MDL2875-0072713.)

17. The FDA communicated to Torrent that it considered these batches adulterated. (*Id.*) Torrent initiated a recall of the five impacted batches and began analyzing the 25 lots of API used in the remaining 103 batches on the market. (*Id.*) Torrent did not analyze API batches used in finished dose product that was not within expiry. (*Id.*)

18. On August 7, 2018, European health authorities inquired with ZHP whether there was a possibility that n-nitrosodiethylamine (NDEA) could be formed during its API manufacturing process. (Torrent Ex. 8, ZHP00496536.) ZHP began developing an analytical method to test its API for NDEA. (*Id.*)

19. On August 18, 2018, the Director of Torrent Pharmaceuticals Ltd. questioned what had been done since Torrent received the notification from ZHP on June 26, 2018, regarding contamination of "D" code valsartan API to "conclude if c batches had any issues or not." (Torrent Ex. 10, TORRENT-MDL2875-00072713 at 2; Torrent Ex. 1, Jaiswal Dep. 110:13–15, 114:20–24, 115:1–20.) Torrent's operations department cited the "declaration" received from its vendor, ZHP. (*Id.*)

20. However, between June 26 and August 18, 2018, Torrent did not perform any of its own testing to confirm the accuracy of ZHP's declaration. (Torrent Ex. 1, Jaiswal Dep. 231:15–18, 239:9–21.) Nonetheless, it is undisputed that Torrent had capacity to develop a test for NDMA given that it did, in fact, develop and use such a test. (*Id.* at 236:11–21.) Torrent admitted that it was under no obligation to wait for ZHP, as the DMF holder, to develop a test for NDMA. (*Id.* at239:9–17.) Ultimately, it took Torrent only about five weeks to develop a test for NDMA. (*Id.* at 245:3–8, 245:18–23.)

21. Torrent initiated its recall of valsartan with valsartan amlodipine hydrochlorothiazide on August 17, 2018. (Torrent Ex. 24, TORRENT-MDL2875-00007721.) This was two weeks after Torrent was notified by ZHP that "old" process API used to make that product was contaminated with NDMA. (Torrent Ex. 11, TORRENT-MDL2875-00131255.)

22. On August 29, 2018, ZHP tested selective valsartan API batches and determined that NDEA was present in valsartan manufactured with triethylamine (the TEA process). (Torrent Ex. 8, ZHP00496536.) Torrent evaluated its valsartan for NDEA after it had initiated a recall of its product for NDMA contamination. (Torrent Ex. 1, Jaiswal Dep. 77:15–17.)

IV. The NDMA/NDEA Contamination Levels in Torrent's Valsartan

23. All of the valsartan manufactured and sold by Torrent in the United States contained NDMA and NDEA. (Torrent Ex. 2, Jaiswal Dep. 386:3–15.)

24. Torrent's Director of Quality, Sushil Jaiswal, and Director of Regulatory Affairs, Dawn Chitty, both confirmed that the level of NDMA carried over into Torrent's finished dose products exceeded the interim limits set by the FDA. (*See*, *e.g.*, Torrent Ex. 9, TORRENT-MDL2875-00133890, Torrent Ex. 12, TORRENT-MDL2875-00366172.) For example:

a. Various batches of product contained 12.3 ppm, 12.88 ppm, 65.29 ppm, and 125.03 ppm NDMA which is 41 times, 42 times, 85 times, 217, and 416 times the acceptable daily limit for NDMA set by the FDA, respectively. (Torrent Ex. 1, Jaiswal Dep. 79:3–14, 81:4–83:11, 84:4–87:2.)

b. Various batches of product contained 7.89 ppm, 14.13 ppm, 15.29 ppm, and 16.93 ppm NDEA which is 95 times, 170 times, 184 times, and 203 times the acceptable daily limit for NDEA set by the FDA, respectively. (*Id.*; Torrent Ex. 3, Chitty 59:15–61:18.)

25. These NDMA and NDEA results reflect the nitrosamine content of batches that Torrent had purchased. (*Id.* at 64:15–19.) The batch numbers from Torrent's own test results demonstrating that the batches of valsartan API it purchased from ZHP contained NDMA and NDEA correspond to the batch numbers from Torrent's finished dose valsartan, demonstrating that contaminated valsartan API was used to make finished dose valsartan. (*Id.* at 65:16–69:10.)

V. Causes of Contamination

26. For D code valsartan API, which is manufactured with the "new" (zinc chloride) process, API manufacturer ZHP concluded "[redacted]":

[redacted]

(Torrent Ex. 8, ZHP00496536.)

27. For C code valsartan API, which is manufactured with the "old" (TEA) process, API manufacturer ZHP concluded "[redacted] (*Id.*). Thus, the reaction mechanism is as follows:

[redacted]

(*Id.*)

28. Though the route of synthesis for C Code valsartan would not suggest high levels of NDMA, both NDMA and NDEA were present in C code valsartan API at levels multiple to hundreds of times the acceptable daily limit set by the FDA. (Torrent Ex. 1, Jaiswal Dep. 79:3–14, 81:4–83:11, 84:4–87:2; Torrent Ex. 3, Chitty Dep. 59:15–61:18.)

29. ZHP reasoned, [redacted] ." (*Id.*)

30. ZHP explained that that while there were dedicated production lines for valsartan API, valsartan API manufactured with different processes (e.g., old process and new process) shared production lines) and "[redacted] ." (*Id.*)

31. Further, ZHP noted that NDMA and NDEA [redacted] ” resulting in contamination o of [redacted] ” (*Id.*) This is because [redacted] creating a [redacted] ” via recovered solvents. (*Id.*)

VI. Torrent’s Representations and Warranties Concerning Its Valsartan

32. Torrent represented at all times that its finished dose valsartan-containing drugs *were* valsartan, valsartan amlodipine, or valsartan amlodipine hydrochloride USP. (Torrent Ex. 25, TORRENT-MDL2875-00003680; Torrent Ex. 22, TORRENT-MDL2875-00269671; Ex. 13, TORRENT-MDL2875-00557249; Torrent Ex. 14, TORRENT-MDL2875-00557247.)

33. Torrent represented at all times that its finished dose valsartan complied with all applicable standards, including identity, strength, quality, and purity standards.

34. In the course of marketing and selling finished dose valsartan in the United States market, Torrent communicated with customers and third-party payors. (Torrent Ex. 4, Gegenheimer Dep. 56:9–18.)

35. The ANDAs filed by Torrent referenced DMF registration number 23491 and the known list of impurities for that process but did not include NDMA, NDEA, or any other nitrosamine. (Torrent Ex. 26, TORRENT-MDL2875-00003433.)

36. In its ANDA submission, Torrent stated that its product complied with applicable quality standards. (Torrent Ex. 7, Rivera Dep. 106:21–107:1.) Additionally, Torrent, in its ANDA submission, stated that its generic valsartan drugs were bioequivalent to the name

brand drug, Diovan. (Torrent Ex. 7, Rivera Dep. 119:2–6; Torrent Ex. 4, Gegenheimer Dep. 244:21–23.)

37. Torrent's valsartan products were designated "USP," which stands for "United States Pharmacopeia." (Torrent Ex. 6, Perry Dep. 177:15–18.) The designation USP indicates that a drug complies with all the testing requirements that are posted in the United States Pharmacopeia for that drug's monograph. (Torrent Ex. 6, Perry Dep. 177:15–21.) It is only if a product meets those standards that a manufacturer "can use the USP after [its] drug name." (Torrent Ex. 6, Perry Dep. 177:21–24.) The valsartan monograph does not include NDMA or NDEA. (Torrent Ex. 15, TORRENT-MDL2875-00232735.) Similarly, the valsartan API Torrent purchased from ZHP was designated as "U.S.P." (Torrent Ex. 2, Jaiswal Dep. 451.9–18.)

38. Torrent represented "At Torrent, we strongly believe in providing quality medicines at affordable price," on its publicly accessible website. (Torrent Ex. 3, Chitty Dep. 16:20–17:14.) According to Dawn Chitty, Torrent USA's Vice President of Regulatory Affairs, "quality" in that context generally [redacted] (*Id.*)

39. Torrent acknowledged that, as the finished dose manufacturer, it is Torrent's duty to follow industry standards regarding genotoxic impurities. (Torrent Ex. 1, Jaiswal Dep. 193:17–21.)

40. Since at least 2015, Torrent provided customers materials stating that there were no hazardous materials or cytotoxic agents involved in valsartan. (Torrent Ex. 4, Gegenheimer Dep. 201:14–202:11.)

41. When other generic manufacturers of valsartan-containing drugs recalled their products due to the presence of nitrosamine impurities on July 13, Torrent represented that its valsartan-containing drugs were not recalled and did not contain nitrosamines. (Torrent Ex. 3, Chitty Dep. 297:7–13, 299:13–300:16.) At the time these representations were made, Torrent had *not* tested its valsartan-containing drugs to confirm that they were free of nitrosamines. (*Id.* at 284:10–19, 287:13–288:9; Torrent Ex. 16, TORRENT-MDL2875-00511197.)

42. Even after ZHP notified Torrent that the "old" (TEA) process API by Torrent to make valsartan for the United States market contained NDMA, Torrent did not immediately test its product. (*Id.*;)

43. From the time that Torrent had first been notified of nitrosamines in "new" process valsartan API on June 26, 2018 through August 3, 2018, Torrent represented that its valsartan did not contain nitrosamines—though it never confirmed this. (*Id.*; Torrent Ex. 17, TORRENT-MDL2875-00555405.) Then, when Torrent learned NDMA was present in "old" process API, it continued to represent that its valsartan-containing drugs were free of impurities and held off on initiating a recall for nearly two-weeks rather than notifying customers. (*Id.*) Even on the *day* the recall was issued, Torrent continued to tell its customers that its valsartan was not recalled. (*Id.*)

VII. Breach of Warranties

44. For a maximum daily dose of 320 mg valsartan/day, the acceptable intake limit for NDMA, set by the FDA, is 96 ng/day, or 0.3 ppm. (Ex. 23.)

45. For a maximum daily dose of 320 mg valsartan/day, the acceptable intake limit for NDEA, set by the FDA is 26.5 ng/day or 0.083 ppm. (*Id.*)

46. Mr. Jaiswal, as Torrent's Head of Quality, testified that its customers "expect a right and quality medicine" and that "pharmaceutical quality," as per the FDA means [redacted] (Torrent Ex. 2, Jaiswal Dep. 685:15–687:2.) He explained that in order for a product, like valsartan, to be "quality" it must be [redacted] and, additionally "[redacted] (*Id.* at 688:5–21.)

47. The recall notices sent by Torrent to customers confirmed the presence of an "impurity" in Torrent's valsartan-containing drugs classified as a "probable human carcinogen" by the International Agency for Research on Cancer (IARC). **(**Torrent Ex. 18, TORRENT-MDL2875-00515246.**)**

48. For all batches of Torrent's valsartan product in the market, the levels of NDMA and NDEA exceeded the acceptable intake levels set by the FDA. (Torrent Ex. 9, TORRENT-MDL2875-00133890, Torrent Ex. 12, TORRENT-MDL2875-00366172.) Torrent had to recall its valsartan product because the FDA considered it adulterated. (Torrent Ex. 13, TORRENT-MDL2875-007213.)

49. Upon initiating a recall of its valsartan for the presence of NDMA, Torrent admitted that NDMA was "classified as a probable human carcinogen." (Torrent Ex. 19, TORRENT-MDL2875-00190373.) Torrent acknowledged [redacted] and "[redacted] (*Id.*) In fact, Torrent stated that "[redacted] (*Id.*)

50. Torrent relied on its API vendor, ZHP, to confirm that its valsartan API was free of genotoxic impurities. (*See*, *e.g.*, Torrent Ex. 1, Jaiswal Dep. 206:7–207:19, 210:3–212:8.) Torrent did not actually test the valsartan API for genotoxic impurities. (*Id.* at 212:5–

213:12.) In fact, Torrent admitted that it did nothing to control for genotoxic impurities in the valsartan API it purchased except to (1) rely on the genotoxicity declaration from ZHP, the API vendor; and (2) review the route of synthesis for genotoxicity alert, even though [redacted] (*Id.* 86:23–88:19.) However, those methods were inadequate:

a. Sushil Jaiswal, Torrent's 30(b)(6) representative agreed that, ultimately, declarations upon which Torrent chose to rely were wrong. (*Id.* 234:24–235:3.)

b. The route of synthesis information, though limited, demonstrated the potential to generate nitrosamines; Mr. Jaiswal further agreed that this potential was apparent well before Torrent sold nitrosamines in the United States, including as early as the 1980s or 1990s. (*Id.* 327:19–328:5.)

III. Torrent's Admissions Regarding cGMP

51. Sushil Jaiswal, Torrent's Head of Quality and Torrent's 30(b)(6) representative agreed that in the pharmaceutical industry, there are several chemical and physical properties to evaluate in a drug substance to satisfy FDA and ICH regulations but "genotoxic impurity control" is the "most significant factor." (Torrent Ex. 2, Jaiswal Dep. 369:6–370:5.)

52. Torrent agreed that one set of applicable regulations is found in the FDA's M7 Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk Guidance for Industry, published in 2015. (Torrent Ex. 1, 371:1–7, 372:12–17, 373:4–8.) Torrent agreed that, at least as of the date of publication of these guidelines, it was necessary to keep genotoxic impurities under the level specified

therein, including specifically for compounds that were part of the "cohort of the concern." (*Id.* 37:12–18, 381:22–382:18.) The "cohort of concern," Torrent agreed, is a [redacted] such as n-nitroso compounds like NDEA and NDMA. (*Id.*)

53. For the cohort of concern, the "threshold of toxicological concern" is lower than the 4.7 ppm threshold of toxicological concern for other genotoxic impurities. (Torrent Ex. 1, Jaiswal Dep. 383:15–386:1.) Torrent's valsartan-containing drugs contained nitrosamines at levels *greater* than 4.7 ppm—the level for impurities *not* included in the cohort of concern. (*Id.* at 386:3–15.) Torrent agreed that lower levels than even 4.7 ppm are required for n-nitroso compounds because they are part of the cohort of concern. (*Id.* at 375:6–377:9, 383:15–386:1.) In other words, Torrent's valsartan contained genotoxic impurities in excess of the threshold of toxicological concern for genotoxic impurities generally and for genotoxic impurities within the cohort of concern (to which NDMA and NDEA belong). The ICH M7 guidance was published in May 2015, at or around the time Torrent began supplying valsartan to the United States market. (*Id.* at 373:4–8.)

54. On behalf of Torrent, Mr. Jaiswal further agreed that genotoxic compounds in a drug "[redacted]." (Torrent Ex. 1, Jaiswal Dep. 52:11–14.) Specifically, it would be important to investigate to make sure the genotoxic compound does not exceed threshold levels. (*Id.* at 53:18–54:1.)

55. Presented with the European Medicines Agency document "Guidelines on the Limits of Genotoxic Impurities" from 2006," Mr. Jaiswal acknowledged on behalf of Torrent that genotoxic compounds, like NDMA, have the potential to damage DNA at any level of exposure. (*Id.* at 55:17–57:4.) Torrent agreed with EMA that for "[redacted]

[redacted] and further agreed that "[redacted]." (*Id.* at 56:16–19, 58:16–22.)

56. Mr. Jaiswal admitted that he was aware of the EMA Guidelines on the Limits of Genotoxic Impurities. (*Id.* at 59:4–9.)

57. Dawn Chitty, Torrent's Head of Regulatory and Scientific Affairs, agreed that if Torrent could not ensure that its drugs met identity, strength, quality, and purity standards, then its drugs would be adulterated and could not be sold. (Torrent Ex. 3, Chitty Dep. 111:15–112:10.) Similarly, Torrent's Regulatory Affairs Manager, Jocelyn Rivera, admitted, however, that it was required to show that its drugs comply with, among other standards, identity, strength, quality, and purity standards. (*Id.* at 112:17–113:17; Torrent Ex. 7, Rivera Dep. 111:24–15.)

58. In an April 2017 Establishment Inspection Report (EIR) for Torrent's manufacturing facilities, the FDA issued FDA 483 observations including that "[redacted]." (Torrent Ex. 7, Rivera Dep. 108:9–111:22.)

59. Following the recall of valsartan-containing drugs for nitrosamine contamination, the FDA and EMA explained that one of the reasons for the contamination was that there was a lack of "good science" on the part of manufacturers; Mr. Jaiswal agreed that Torrent lacked good science leading up to the recall. (Torrent Ex. 2, Jaiswal Dep. 672:17–673:17.)

60. In its ANDA for valsartan, Torrent was required to state that the drug satisfied strength, identity, quality, and purity standards. (Torrent Ex. 3, Chitty Dep. 115:21–116:2.)

61. Dawn Chitty, Torrent's head of Regulatory and Scientific Affairs, testified that "any type of situation that potentially could impact [Torrent's] products should be investigated" and that responsibility also means Torrent is "obligated to test API." (*Id.* at 127:8–128:4.)

IV. Torrent's Financial Focus

62. After ZHP had notified Torrent that its "new" process valsartan contained NDMA, ZHP and Torrent discussed minimizing the profits they would lose due to the genotoxic contamination, stating: "[redacted]." (*see* Torrent Ex. 20, TORRENT-MDL2875-00090456.)

63. Rather than testing its product for nitrosamine contamination (Torrent Ex. 20, Torrent Ex. 1, Jaiswal Dep. 23:41–1–10, 230:4–17.) Torrent internally discussed how nitrosamine contamination would affect Torrent financially (Torrent Ex. 21, TORRENT-MDL2875-00072542.). For example, on July 17, 2018, Torrent's Chief Operating Officer wrote an email stating, "[redacted]…" (*Id.*; Torrent Ex. 3, Chitty Dep. 245:3–246:11; *see also* Torrent Ex. 20, TORRENT-MDL2875-00090456.)